Remarks

New claims 23-24 have been added. No new matter is added. Claim 23 depends from claim 1 and further limits what the α-amino acid could be. The Examiner contends in the Advisory Action that claim 24 fails to further limit the subject matter of claim1, since it includes the composition containing the combination of glycine and a 4-amino-3-substituted butanoic acid derivative wherein R_2 is phenyl or naphthyl which is mono-, di- or tri-substituted with a halogen atom. Applicants respectfully disagree. Claim 24 limits the α-amino acid to glycine, and further limits "R_2", i.e. where R_2 is phenyl or naphthyl mono-, di- or trisubstituted, the substituent "halogen" has now been omitted. The Examiner's attention is drawn to page 6 of this response.

Similarly, in the Office Action, the Examiner has objected to claims 2-9 as being of improper dependent form for failing to further limit the subject matter of a previous claim; specifically, claim 1 recites that the required element of an α-amino acid cannot be glycine, and claims 2-9 are drawn to an alpha-amino acid that can be glycine. For analagous reasons, the claims have been rejected under 35 U.S.C. § 112. While Applicants agree that dependent claims 2-9 are drawn to an α-amino acid that *can* be glycine, these claims carry with them the same limitations of claim 1, i.e. that the α-amino acid cannot be glycine only when *R_2 is a phenyl or naphthyl group which is mono-, di- or tri-substituted with a halogen atom.* In all other instances, the α-amino acid can be glycine, and claims 2-9 are consistent in this respect. For this reason, withdrawal of the objection and the § 112 rejection is respectfully requested.

The Examiner has rejected claims 1-8 as being anticipated by Robson. Robson teaches a composition comprising baclofen and glycine. As stated above, the instant

claims require that when R_2 is a phenyl or naphthyl group which is mono-, di- or tri-substituted with a halogen atom, the α-amino acid is not glycine. Baclofen is a 4-amino-3-substituted-butanoic acid in which R_2 is 4-chlorophenyl and R_1 is hydrogen. Therefore, the cited reference does not anticipate the pharmaceutical preparation of the instant claims.

Claim 1 has been amended such that when the 4-amino-3-substituted-butanoic acid derivative is gabapentin, the α-amino acid is not methyl-D-aspartic acid. A marked-up copy of claim 1 is included herewith. Woodruff teaches a solution comprising N-methyl-D-aspartic acid and gabapentin. As such, the instant claims are not anticipated by the Woodruff reference.

In the Advisory Action, the Examiner contends that no support exists for a proviso such as "provided that when the 4-amino-3-substituted-butanoic acid derivative is gabapentin, the α-amino acid is not methyl-D-aspartic acid," and has rejected the claim based on the fact it raises an issue of new matter. Applicants respectfully submit that the addition of this proviso does not contain new matter. Specifically, the Examiner has not carried his burden of supplying a sufficient factual basis to support a conclusion that the negative limitation in question introduces a new concept into the application disclosure. *Ex Parte Ivo G. Dalla Lana and Karl Tze-Tang Chuang*, 2002 WL 31321761, 2 (citing *In Re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992)); it is merely stated that such a proviso was "never contemplated".

In fact, the specification as filed reasonably conveys to one skilled in the art that Applicants had possession of the proviso that when the 3-amino-4-butanoic acid derivative is gabapentin, the α-amino acid is not methyl-D-aspartic acid. Initially, the

specification identifies gabapentin as one example of a 3-amino-4-butanoic acid derivative. Further, methyl-D-aspartic acid is disclosed as a possible α-amino acid (see, for example, the text at page 38, lines 23-26). It follows that the specification, having described the whole, i.e. an α-amino acid supported by the examples found on pages 38-39, necessarily describes the part remaining, i.e. all other α-amino acids except methyl-D-aspartic acid, when the 3-amino-4-butanoic acid is gabapentin (support for the 3-amino-4-butanoic acid being gabapentin is found throughout the entire specification, including the working examples). *In Re Johnson*, 558 F.2d 1008, 1019 (Cust. & Pat..App. 1976).

Applicants also point out that such a negative limitation need not be expressly set forth in the specification. *Ex Parte Lana and Chuang*, 2002 WL 31321761, 2. It is enough that the specification as a whole, including the examples provided therein, reasonably conveys to a person skilled in the art that Applicants had possession of the proviso in question at the time the present application was filed. *id.* Applicants distinctly list methyl-D-aspartic acid as a possible α-amino acid. In addition, the present application contains *eight* working examples (see Examples 1-8) of compositions wherein gabapentin is the 3-amino-4-butanoic acid, and methyl-D-aspartic acid is *never* the α-amino acid. Applicants submit that this is sufficient support for the notion that, although the α-amino acid *can* be methyl-D-aspartic acid in the instant invention, Applicants *never* intended for it to be methyl-D-aspartic acid when the 3-amino-4-butanoic acid is gabapentin.

Applicants also direct the Examiner's attention to page 2 of the specification, which cites the Woodruff patent, U.S. Patent No. 5,084,479 in the background section.

As Applicants were aware of the state of the art at the time the application was filed, i.e. a composition containing gabapentin and methyl-D-aspartic acid, Applicants would not want to claim such subject matter. In view of the above arguments, withdrawal of the new matter rejection is respectfully requested.

Allowance of the claims and passage of the case to issue are respectfully solicited. The Applicants urge the Examiner to contact the Applicants' undersigned representative at (312) 913-0001 if he believes that this would expedite prosecution of this application.

Respectfully submitted,

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Dated: December 2, 2002

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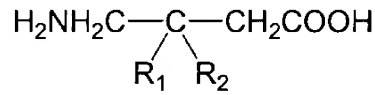
Marked-Up Copy of Claims for U.S.S.N. 09/674,815

Claim 1 has been amended as follows.

1. (Twice Amended) A stabilized pharmaceutical preparation, comprising: (a) and α amino acid; (b) an optional auxiliary agent for manufacturing a pharmaceutical preparation; and (c) a 4-amino-3-substituted-butanoic acid derivative, which 4-amino-3-substituted-butanoic acid derivative has the general formula:



wherein,

R_1 is a hydrogen atom, a hydroxyl group, a methyl group or an ethyl group;

R_2 is a monovalent group selected from:

a straight or branched alkyl group of 3 - 8 carbon atoms;

a straight or branched alkylene group of 3 - 8 carbon atoms;

a straight or branched alkyl group of 3 - 8 carbon atoms which is mono- or di-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, an oxo group, a carboxyl group or a carboalkoxy group;

a cycloalkyl group of 3 - 8 carbon atoms;

a cycloalkyl group of 3 - 8 carbon atoms which is mono-, di- or tri-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, an oxo group, a carboxyl group or a carboalkoxy group;

a condensed ring group formed by ortho-fusion of a phenyl ring with a cycloalkyl group of 4 - 8 carbon atoms;

a condensed ring group formed by ortho-fusion of a phenyl ring with a cycloalkyl group of 4 - 8 carbon atoms wherein said phenyl ring is mono-, di- or tri-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, a carboxyl group or a carboalkoxy group;

a condensed ring group formed by ortho-fusion of a phenyl ring with a cycloalkenyl group of 5 - 8 carbon atoms or a cycloalkanedienyl group of 5 - 8 carbon atoms;

a condensed ring group formed by ortho-fusion of a phenyl ring with a cycloalkenyl group of 5 - 8 carbon atoms or a cycloalkanedienyl group of 5 - 8 carbon atoms wherein said phenyl ring is mono-, di- or tri-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, a carboxyl group or a carboalkoxy group;

an alkylcycloalkyl group wherein said cycloalkyl has 3 - 8 carbon atoms and is linked to an alkylene group having 1 - 4 carbon atoms optionally interrupted with -O-, -S- or -SS-;

an alkylcycloalkyl group wherein said cycloalkyl has 3 - 8 carbon atoms, is linked to an alkylene group having 1 - 4 carbon atoms optionally interrupted with -O-, -S- or -SS- and is mono-, di- or tri-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, an oxo group, a carboxyl group or a carboalkoxy group;

a cycloalkyl group of 5 - 8 carbon atoms wherein one of the methylene groups ($-CH_2-$) is replaced by -O-, -NH-, -S-, -SO- or $-S(O)_2-$;

a cycloalkyl group of 5 - 8 carbon atoms wherein one of the methylene groups ($-CH_2-$) is replaced by -O-, -NH-, -S-, -SO- or $-S(O)_2-$, and one or two of the unsubstituted methylene groups ($-CH_2-$) are mono- or di-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, an oxo group, a carboxyl group or a carboalkoxy group;

a cycloalkenyl group of 5 - 8 carbon atoms or a cycloalkanedienyl group of 5 - 8 carbon atoms, one of the methylene groups ($-CH_2-$) in said cycloalkenyl ring or cycloalkanedienyl ring being replaced by -O-, -NH-, =N-, -S-, -SO- or $-S(O)_2-$;

a cycloalkenyl group of 5 - 8 carbon atoms or a cycloalkanedienyl group of 5 - 8 carbon atoms, one of the methylene groups ($-CH_2-$) in said cycloalkenyl ring or cycloalkanedienyl ring being replaced by -O-, -NH-, =N-, -S-, -SO- or $-S(O)_2-$, and one or two of the unsubstituted methylene groups ($-CH_2-$) being mono- or di-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, an oxo group, a carboxyl group or a carboalkoxy group;

a condensed ring group formed by ortho-fusion of a phenyl ring with a cycloalkyl group of 5 - 8 carbon atoms wherein one of the methylene groups ($-CH_2-$) is replaced by -O-, -NH-, -S-, -SO- or $-S(O)_2-$;

a condensed ring group formed by ortho-fusion of a phenyl ring with a cycloalkyl group of 5 - 8 carbon atoms wherein one of the methylene groups ($-CH_2-$) is replaced by -O-, -NH-, -S-, -SO- or $-S(O)_2-$, said phenyl group being mono- or di-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, a carboxyl group or a carboalkoxy group;

a condensed ring group formed by ortho-fusion of a phenyl ring with a cycloalkenyl group of 5 - 8 carbon atoms or a cycloalkanedienyl group of 5 - 8 carbon atoms, one of the methylene groups ($-CH_2-$) in said cycloalkenyl ring or cycloalkanedienyl ring being replaced by -O-, -NH-, =N-, -S-, -SO- or $-S(O)_2-$;

a condensed ring group formed by ortho-fusion of a phenyl ring with a cycloalkenyl group of 5 - 8 carbon atoms or a cycloalkanedienyl group of 5 - 8 carbon atoms, one of the methylene groups ($-CH_2-$) in said cycloalkenyl ring or cycloalkanedienyl ring being replaced by -O-, -NH-, =N-, -S-, -SO- or -S(O)2-, said phenyl ring being mono- or di-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, a carboxyl group or a carboalkoxy group;

an alkylcycloalkyl group wherein said cycloalkyl has 5 - 8 carbon atoms and is linked to an alkylene group having 1 - 4 carbon atoms optionally interrupted with -O-, -S- or -SS-, one of the methylene groups ($-CH_2-$) in said cycloalkyl ring being replaced by -O-, -NH-, -S-, -SO- or $-S(O)_2-$;

an alkylcycloalkyl group wherein said cycloalkyl has 5 - 8 carbon atoms and is linked to an alkylene group having 1 - 4 carbon atoms optionally interrupted with -O-, -S- or -SS-, and one of the methylene groups ($-CH_2-$) in said cycloalkyl ring being replaced by -O-, -NH-, -S-, -SO- or $-S(O)_2-$ and one or two of the unsubstituted methylene groups ($-CH_2-$) being mono-, di- or tri-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, an oxo group, a carboxyl group or a carboalkoxy group;

a phenyl or naphthyl group;

a phenyl group substituted with a methylenedioxy group;

a phenyl or naphthyl group which is mono-, di- or tri-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an amino group, a nitro group, a carboxyl group, a phenoxy group, a phenylmethoxy group, a phenylmethoxy group wherein said phenyl ring is mono-substituted with a halogen atom, trifluoromethyl group, an alkoxy group, an amino group, a nitro group, a carboxyl group or a carboalkoxy group, a cycloalkylmethoxy group having 5 - 8 carbon atoms in the cycloalkyl ring, a cycloalkenylmethoxy group having 5 - 8 carbon atoms in the cycloalkenyl ring, a cycloalkanedienylmethoxy group having 5 - 8 carbon atoms in the cycloalkanedienyl ring, a cycloalkylmethoxy group wherein one of the methylene groups ($-CH_2-$) in said cycloalkyl ring having 5 - 8 carbon atoms is replaced by -O-, -NH-, -S-, -SO- or $-S(O)_2-$, a cycloalkenylmethoxy group wherein one of the methylene groups ($-CH_2-$) in said cycloalkenyl ring having 5 - 8 carbon atoms is replaced by -O-, -NH-, =N-, -S-, -SO- or $-S(O)_2-$, a cycloalkanedienyl-methoxy group wherein one of the methylene groups ($-CH_2-$) in said cycloalkanedienyl ring having 5 - 8 carbon atoms is replaced by -O-, -NH-, =N-, -S-, -SO- or $-S(O)_2-$ group, a cycloalkylmethoxy group having 5 - 8 carbon atoms in the cycloalkyl ring wherein said cycloalkyl ring is mono-substituted with a halogen atom, trifluoromethyl group, a hydroxy group, an alkyl group, an alkoxy group, an amino group, a nitro group, a carboxyl group or a carboalkoxy group

and one of the methylene groups ($-CH_2-$) in said cycloalkyl ring is replaced by -O-, -NH-, -S-, -SO- or $-S(O)_2-$, a cycloalkenylmethoxy group having 5 - 8 carbon atoms in the cycloalkenyl ring wherein said cycloalkenyl ring is mono-substituted with a halogen atom, a trifluoromethyl group, a hydroxy group, an alkyl group, an alkoxy group, an amino group, a nitro group, an oxo group, a carboxyl group or a carboalkoxy group and one of the methylene groups ($-CH_2-$) in said cycloalkenyl ring is replaced by -O-, -NH-, =N-, -S-, -SO- or $-S(O)_2-$, or a cycloalkanedienylmethoxy group having 5 - 8 carbon atoms in the cycloalkanedienyl ring wherein said cycloalkanedienyl ring is mono-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an amino group, a nitro group, an oxo group, a carboxyl group or a carboalkoxy group and one of the methylene groups ($-CH_2-$) in said cycloalkanedienyl ring is replaced by -O-, -NH-, =N-, -S-, -SO- or $-S(O)_2-$;

an alkylphenyl group wherein said phenyl group is linked to an alkylene group having 1 - 4 carbon atoms optionally interrupted with -O-, -S- or -SS-;

an alkyl-O-, -S- or -SS-phenyl group wherein said phenyl group is linked to an alkylene group having 1 - 4 carbon atoms via -O-, -S- or -SS-;

an -O-, -S- or -SS-phenyl group;

a diphenylamino group;

an alkylphenyl group wherein said phenyl group is linked to an alkylene group having 1 - 4 carbon atoms optionally interrupted with -O-, -S- or -SS- and mono-, di- or tri-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, a alkyl group, an alkoxy group, an amino group, a nitro group or a carboxyl group;

an alkyl-O-, -S- or -SS-phenyl group wherein said phenyl group is linked to an alkylene group having 1 - 4 carbon atoms via -O-, -S- or -SS- and mono-, di- or tri-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an amino group, a nitro group or a carboxyl group;

an -O-, -S- or -SS-phenyl group wherein said phenyl group is mono-, di- or tri-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an amino group, a nitro group or a carboxyl group;

or

R_1 and R_2, together with the carbon atom to which they are attached, may form a divalent group selected from:

a cycloalkylidene group of 5 - 8 carbon atoms;

a cycloalkylidene group of 5 - 8 carbon atoms which is mono-, di-, tri- or tetra-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, a cycloalkyl group, a phenyl group, an amino group, a nitro group or a carboxyl group;

a cycloalkylidene group of 5 - 8 carbon atoms wherein one of the methylene groups ($-CH_2-$) in said cycloalkyl ring is replaced by -O-, -NH-, -S-, -SO- or $-S(O)_2-$;

a cycloalkylidene group of 5 - 8 carbon atoms wherein one of the methylene groups ($-CH_2-$) in said cycloalkyl ring is replaced by -O-, -NH-, -S-, -SO- or $-S(O)_2-$ group and one or more of the unsubstituted methylene groups ($-CH_2-$) in said cycloalkyl ring are mono-, di-, tri- or tetra-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, an oxo group, a carboxyl group or a carboalkoxy group;

a cycloalkenylidene group of 5 - 8 carbon atoms or a cycloalkanedienylidene group of 5 - 8 carbon atoms;

a cycloalkenylidene group of 5 - 8 carbon atoms or a cycloalkanedienylidene group of 5 - 8 carbon atoms which is mono-, di-, tri- or tetra-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, a cycloalkyl group, a phenyl group, an amino group, a nitro group, an oxo group, a carboxyl group or a carboalkoxy group;

a cycloalkenylidene group of 5 - 8 carbon atoms or a cycloalkanedienylidene group of 5 - 8 carbon atoms wherein one of the methylene groups ($-CH_2-$) in said cycloalkenyl ring or cycloalkanedienyl ring is replaced by -O-, -NH-, =N-, -S-, -SO- or $-S(O)_2-$;

a cycloalkenylidene group of 5 - 8 carbon atoms or a cycloalkanedienylidene group of 5 - 8 carbon atoms wherein one of the methylene groups ($-CH_2-$) in said cycloalkenyl ring or cycloalkanedienyl ring is replaced by -O-, -NH-, =N-, -S-, -SO- or $-S(O)_2-$ group and one or more of the unsubstituted methylene groups ($-CH_2-$) in said cycloalkenyl ring or cycloalkanedienyl ring are mono-, di-, tri- or tetra-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, an oxo group, a carboxyl group or a carboalkoxy group;

a condensed ring group formed by ortho-fusion of a phenyl ring with a cycloalkylidene group of 4 - 8 carbon atoms;

a condensed ring group formed by ortho-fusion of a phenyl ring with a cycloalkylidene group of 4 - 8 carbon atoms, said phenyl ring being mono-, di-, tri- or tetra-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, a carboxyl group or a carboalkoxy group;

a condensed ring group formed by ortho-fusion of a phenyl ring with a cycloalkenylidene group of 5 - 8 carbon atoms or a cycloalkanedienylidene group of 5 - 8 carbon atoms;

a condensed ring group formed by ortho-fusion of a phenyl ring with a cycloalkenylidene group of 5 - 8 carbon atoms or a cycloalkanedienylidene group of 5 - 8 carbon atoms, said phenyl ring

being mono- or di-substituted with a halogen atom, a trifluoromethyl group, a hydroxyl group, an alkyl group, an alkoxy group, an alkylthio group, an amino group, a nitro group, a carboxyl group or a carboalkoxy group; ~~or~~

provided that when R_2 is a phenyl or naphthyl group which is mono-, di- or tri-substituted with a halogen atom, the α-amino acid is not glycine; and

provided that when the 4-amino-3-substituted-butanoic acid derivative is gabapentin, the α-amino acid is not methyl-D-aspartic acid.